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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/661,580	09/15/2003	Katsuya Kishikawa	Q77518	8051

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EXAMINER	
KWON, BRIAN YONG S	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 12/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/661,580	KISHIKAWA ET AL.	
	Examiner	Art Unit	
	Brian S. Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,3,5 and 6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,3,5 and 6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 10/030,314.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *07/19/05, 09/15/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This application discloses and claims only subject matter disclosed in prior Application No.10/030,314, filed 01/10/2002, and names an inventor or inventors named in the prior application. Accordingly, this application may constitute a continuation or division. Should applicant desire to obtain the benefit of the filing date of the prior application, attention is directed to 35 U.S.C. 120 and 37 CFR 1.78.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 2-3 and 5-6 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating pulmonary fibrosis with the administration of sphingosine-1-phosphate, does not reasonably provide enablement for "preventing and/or treating a fibrosis" or "interstitial pneumonia, chronic hepatitis, hepatic cirrhosis, chronic renal failure or renal failure" with sphingosine 1-phosphate receptor agonist or sphingosine 1-phosphate. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of

the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

The claims are broadly directed to a method for preventing and/or treating a fibrosis comprising administering a sphingosine 1-phosphate receptor agonist, wherein claims 3 and 6 further limit the fibrosis as "pulmonary fibrosis, interstititial pneumonia, chronic hepatitis, hepatic cirrhosis, chronic renal failure or renal glomerulosclerosis; and wherein claim 5-6 further limit the sphingosine 1-phosphate receptor agonist as sphingosine 1-phosphate.

Sphingosine 1-phosphate (S1P) is known to elicit a wide spectrum of biological responses in cells including mitogenesis, cell-shape changes, migration and contraction. Edg-1, Edg-3, Edg-5, Edg-6 and Edg-8 are known as specific S1P receptors. It is also known that Edg-1, Edg-5 and Edg-6 are expressed in the lungs, and Edg-1, Edg-3 and Edg-5 are expressed in the liver and kidney.

Although the specific S1P receptors (e.g., Edg-1, Edg-3, Edg-5, Edg-6 and Edg-8) are known to be expressed in various organs including lungs, liver and kidney, the art is silent about whether the administration of any compound having S1P agonist property would non-selectively modulate activity in all subtypes of S1P receptors and provide the utility of claims directed to fibrosis in disparate types of organs. Since it is generally known in the art that each specific subtype of receptor has unique biologic activity, proof must be provided that the applicant's assertion has merits.

With respect to the instantly claimed "prevention of fibrosis", the state of art does not recognize the administration of any compounds or compositions to prevent or completely eliminate (cure) the fibrosis, for example pulmonary fibrosis, chronic hepatitis, chronic renal failure as required in the instant claims (see "Medical Encylopeia:Idiopathic Pulmonary Fibrosis", Medline Plus, 2004; "Medical Encyclopedia: Chronic Renal Failure", Medline Plus, 2005; "Hepaptitis C", DrugDigest, 2005). Since the applicant's assertion is contrary to what is known in medicine, evidence must be provided that this revolutionary assertion has merits.

The relative skill of those in the art of pharmaceuticals is high. The specification does not provide any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use of the instantly claimed compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

The instant claims embrace the prophylactic or therapeutic treatment of fibrosis ("the formation of excessive fibrous tissue", see the American Heritage Dictionary, Second College Edition, 1982) regardless of involvement of different subtypes of S1P receptor modulation in different organs. In other words, the instant claims cover the prevention (cure or total elimination) or therapeutic treatment of the formation or development of excess fibrous connective tissue in any organ or tissue (e.g., pulmonary fibrosis, endomyocardial fibrosi, cystic fibrosis) including any associated diseases (e.g., chronic renal failure, renal glomerulosclerosi, hepatic cirrhosis, chroic hepatitis, interstitial pneumonia). Furthermore, the instant "sphingosine

1-phosphate receptor agonist" covers any compound that are known to exist and those that may be discovered in the future, for which there is no enablement provided.

In the instant case, sphingosine 1-phosphate is disclosed as the only example of the suitable "sphingosine 1-phosphate receptor agonist", and tested for its efficacy in treating bleomycin-induced lung fibrosis in mice study.

As discussed above, although the specification provide enabling disclosure for therapeutic treatment of using sphingosine 1-phosphate in lung fibrosis, none of the specification provides enabling disclosure for the claimed prophylactic treatment (prevention) of said disorders or prophylactic treatment or therapeutic treatment of the entire scope of fibrosis condition. There is no demonstrated correlation that the tests and results apply to all of the disorders embraced by the instant claims.

As discussed above, the specification fails to provide sufficient guidance in making/using vast number of possible compounds having sphingosine 1-phosphate for the treatment or prevention of said disorders related fibrosis. Furthermore, the specification provides no guidance, in the way of enablement for the full scope of all compounds that are potentially suitable for the invention work similarly as to sphingosine 1-phosphate. The skill artisan would have not known that which compounds of the claimed "sphingosine 1-phosphate receptor agonist" are capable of accomplishing the desired result of the claimed invention without undue amount of experimentation.

Since the efficacy of said compounds in preventing or treating various disorders associated with fibrosis mentioned above cannot be predicted from a priori but must be determined from the case to case by painstaking experimental study and when the above factors

are weighed together, one of ordinary skill in the art would be burdened with undue "painstaking experimentation study" to use the invention commensurate in scope with the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 2-3 and 5-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Spiegel (US 5712262).

The claims read on the prophylactic utility of said sphingsine 1-phoaste receptor agonist, namely sphingosine 1-phosphate.

Spiegel teaches use of sphingosine 1-phosphate in retarding apoptosis in degenerative disease such as ischemic stroke.

Although either Spiegel is silent about said prophylactic utility of sphingosine 1-phosphate, such prophylactic utility deems to be inherent the referenced method. The prior art method administering the same compound to a subject inherently possessing therapeutic utility for the same ultimate purpose as disclosed by the applicant anticipates the claimed invention even absent the claimed property. Applicant's attention is directed to Ex parte Novitski 126 USPQ 1389 (BOPA 1993) illustrating anticipation resulting from inherent use, absent a haec verba recitation for such prophylactic utility. In the instant case, as in Ex parte Novitski, the claims are directed to preventing a malady or disease with old and well known compounds of

compositions. The prior art administering compounds inherently possessing a protective utility anticipates claims directed to such protective use.

Conclusion

4. No Claim is allowed.

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached on (571) 272-0951. The fax number for this Group is (571) 273-8300.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Brian Kwon
Patent Examiner
AU 1614